REMARKS

Reconsideration is respectfully requested in light of the foregoing amendments and following remarks. Entry of the amendment is respectfully requested since it would reduce the issues on appeal and does not introduce new matter.

Claims 1-4 and 6-9 are pending, upon entry of the amendment.

Claims 1, 6 and 7 are amended. Claim 1, as amended, more clearly distinguishes over the combined teachings of the applied references. Claims 6 and 7 are amended to correct dependency. Support for the amendments are to be found in Table 6 is to be found on page 40, and page 37 through line 18 on page 40.

The specification, as requested, has been is again amended to correct the informality noted by the Examine.

A signed Rule 67 declaration will be submitted upon its receipt.

A suitable specification will be submitted upon an indication of allowable subject matter.

The withdrawal of the rejection of claims 1-4 under 35 USC 112, first paragraph, is noted with appreciation.

Rejections under 35 USC 112, Second Paragraph

Claims 1-4 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out distinctly claim containing subject matter which applicant regards as his invention. Applicant respectfully traverses.

Claim 1 has been amended to refer to a proteosome-gp160 complex. See page 39 starting at line 15 for support for this description. See Table 6 and the passage starting at as support for the additional characteristics.

In light of the amendments, withdrawal of the rejection is respectfully requested.

Rejections under 35 USC 103

Claims 1-4 are rejected under 35 USC 103 as being unpatentable over Lowell *et al.* (U) or Lowell *et al.* (V) or Smith *et al.* (W) or Avraham *et al.* (X) in view of Ratner *et al.* (Y). Applicant respectfully traverses.

Applicant again submits that the rejection as framed employs an obvious-to-try rationale. As noted by the Examiner, the primary references do not teach gp160 but merely teach the use proteosomes in a vaccine context. Ratner is cited for its teaching of the existence of gp160. The Examiner states that Ratner *et al.* teach the complete genome of HIV (HTLV-III) including the sequence of gp160.

The Examiner then proposes that since envelope proteins of viruses are antigenic, it would have been obvious to first isolate and purify gp160 and then employ it as the "antigenic" protein/polypeptide in the process and compositions taught by the primary references.

It is submitted that there is a high degree of unpredictability in the vaccine, immunology arts. With regard to an expectation of success, none of the primary references are concerned with the antigenic material of a retrovirus nor do they suggest a reasonable expectation of obtaining the results shown in Table 6. These results are not a miniscule antigenic response. Please consider the enhanced levels shown in the Table, 1.8 (claims 3, and 4) to 3.5 fold of the base value (gp160/alum).

Furthermore, it is not at all to be predicted that after the biochemical and biophysical process manipulations necessary for the formation of the proteosome-gp160 vaccine complexes described, that the fine antigenic structure of such complex protein antigens such as gp160 will be maintained in such a manner as they are able to induce, when so formulated with proteosomes, enhanced immune responses that recognize not only the native protein but also a significant epitope contained within the native protein, as shown in Table 6. The native non-manipulated protein, even with an adjuvant such as alum, may be antigenic but nevertheless be insufficiently immunogenic without the enhanced formulation of the instant invention.

Moreover, unlike simple peptides or proteins which may retain their simple structure, it is not necessary or obvious that a complex protein with intricate three-dimensional structure such as gp160 which consists of components of gp120 and gp41, will, after the formulation processes described in the instant invention with proteosomes, maintain such structure so as to elicit enhanced immunogenicity to both the protein and a critical epitope after being subjected to the formulation processes described. Indeed, it is well known in the art that other formulation processes may denature or degrade the protein so as to impede the induction of antibodies that recognize the original non-denatured protein or certain epitopes therein. In fact, one of the discoveries of the instant invention shown herein is that even complex proteins such as gp160,

will elicit enhanced immune responses after formulation in the manner disclosed. This would not be predicted by the primary references nor by Ratner et al. Ratner et al. simply describes the genome of the protein and no more. There is no teaching in Ratner et al. that suggests that after manipulation and treatment in the manner disclosed that antigenicity could be maintained and its immunogenicity enhanced.

Therefore, it would not have been expected that induction of enhanced levels of antibodies to the gp160, to the gp41 portion of gp160 and to a significant epitope of the protein would result from formulation with proteosomes as described herein. This is especially so since it is known that association between the gp41 and gp120 portions of the gp160 that exists in the native protein, can be disassociated and that therefore potential non-covalent interactions between the such portions of the gp160 or of the entire gp160 and the proteosomes of the instant invention would be expected to have been impeded. It was applicant's discovery that this was did not occur. The instant claimed invention enhances the immunogenicity of the gp160 protein and induces enhanced levels of significant antibodies. In summary, without the experimentation performed by Applicant, it would not have been expected that the proteosome technology would have been effective with complex proteins such as gp160.

In light of these is, it is submitted that a proper *prima facie* case has not been established and the rejection withdrawn. This is respectfully requested.

Further, it is noted that all the primary references were published after the date of the earliest parent application, U.S. Serial No. 07/065,440 ('440 application), filed June 23, 1987. (The use of proteosome-protein complexes is disclosed in the context of a vaccine for AIDS and other HTLV-related diseases. See section bridging pages 22 and 23 of the parent specification. There is no mention of gp 160 per se) Further, it is noted that applicant is listed as a co-author on each of the primary references. As requested by the Examiner, a copy of the '440 application is enclosed.

Conclusion

Having addressed all the rejections and objections, allowance of the application is believed to be in order. A notice to this effect is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 21-0380** referencing docket no. 378332000110. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: December 22, 1999 By: _____

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